REMARKS/ARGUMENTS

Claims 1-12 are pending in the application.

Claims 1-12 stand rejected.

Claims 4-11 stand objected.

Claims 1-12 have been cancelled.

Claims 13-26 have been added and accordingly are new.

Claims 13-24 basically replace original claims 1-12 so as to render the rejections under 35 USC 112 moot. Claim 25 has been added to include a method of manufacturing microarrays and claim 26 have also been added to include an additional method of manufacturing.

CLAIM OBJECTIONS

Claims 4-11 stand objected to under 37 CFR 175 (c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. New claims 16-24 have been added and it is believed that those new claims render moot the objection.

THE REJECTION UNDER 35 U.S.C. 112 SECOND PARAGRAPH

Claims 1-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is believed that by the filing of the new claims that all the rejections and objections under 35 USC 112 first and second paragraphs have been rendered moot.

Applicant has now used the language suggested by the Examiner i.e., using method steps and also introducing the term " to obtain a solution of nucleic acids". Also the terms applying and binding have now been introduced into the independent claims.

Claim 12 stands rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e. results in a claim which is not a proper process claim under 35 U.S.C. § 101. New claim 24 now replaces claim 12, which uses the proper language as suggested by the Examiner.

THE REJECTION UNDER 35 U.S.C. § 102(b)

The rejection of Claims 1-3, 5 and 12 under 35 U.S.C. § 102 (b) as being anticipated by Cronin et al (U.S. Patent No.6,045,996, issued 4 April 2000) is respectfully traversed.

In issuing the outstanding office action, The Examiners' states the following:

"With respect to claim 1, Cronin et al disclose a process for binding nucleic acids to a carrier wherein the nucleic acids are dissolved in a solvent containing at least one betaine, applying the nucleic acid-betaine solution to the carrier whereby the nucleic acids are bound to the carrier i.e. via hybridization to a probe immobilized on the carrier (Column 10, line 48-Column 11, line 20).

Regarding claim 2, Cronin et al. disclose the process wherein the betaine is trimethylmammoium acetate (Column 4, lines 22-31), and regarding Claim 3, Cronin et al. disclose the process wherein the betaine is present at a concentration of 8mM to 6.5M (Column 4, lines 3-31 and Column 5, lines 11-12).

Regarding Claim 5, Cronin et al. disclose the use of betaines as additives for solvents in which nucleic acids are dissolved in order to bind them to a carrier i.e. via hybridization to probe immobilized on the carrier (Column 10, line 48-Column 11, line 20)."

According to the present invention as defined in new claim 13, the nucleic acids and at least one compound selected from the group consisting of betaines are dissolved in a spotting solution. The term "spotting solution" is fully supported by the specification, is the solvent for the nucleic acid and the betaines, see for instance page 5, lines 1 and 2 of the specification. On page 4, first paragraph of the specification, it is disclosed that "*betaines can be added to the solvent after the nucleic acids are dissolved therein*". Thus, it is clearly disclosed in the specification that betaines and nucleic acids are dissolved in the spotting solution.

The present invention as now claimed (new claims 13-26) in the newly presented claims is novel and based on an inventive step and clearly distinguishable over Cronin et al. (US Patent No. 6,045,996, issued April 4, 2000).

Cronin et al. describes in the abstract and specification "*methods of performing nucleic acid hybridization assays on high-density substrate-bound oligonucleotide arrays involving including in the hybridization mixture and isostabilizing agent, a denaturing agent or a renaturation accerlerant*". According to column 3, lines 32 to 37 of Cronin et al., "*a hybridization mixture containing the target and an isostabilizing agent..... is brought into contact with the probes of the array and incubated at a temperature and for a time appropriate to allow hybridization between the target and any complementary probes*". The terms "probe" and "target" are defined in column 2, lines 58 to column 8, lines 8 of Cronin et al. The "probe" is " *a surface-immobilized oligonucleotide that can be recognized by a particular target*". This means that the "probes" are the nucleic acids, which are bound onto the surface of a DNA microarray. The "target" is defined in Cronin et al, as " *a nucleic acid molecule that has an affinity for a given probe*". According to Cronin et al., "*betaines*" *are used as isostabilizing agents*", see column 4, lines 7 to 9.

In other words, Cronin et al. teaches that the nucleic acids to be investigated and a betaine are contacted with a microarray (a support having immobilized on its surface a nucleic acid complementary to the nucleic acid to be investigated). The nucleic acid to be investigated is hybridized to the nucleic acid of the array. Furthermore, Cronin et al. teaches the use of arrays in hybridizing the target nucleic acid to it with the help of a betaine but not the production of arrays or the binding of the nucleic acid to a carrier or to the surface of the microarray.

In contradistinction, the instant invention is directed to the spotting and binding of nucleic acids onto a carrier by using betaines. In the spotting and binding process of the invention, probes are immobilized onto the carrier, i.e. microarrays are produced. The spotting and binding process of nucleic acids to a carrier as claimed in the instant invention is very different from the hybridization method described in Cronin, et al. With the spotting and binding process of the invention microarrays are produced. In the hybridization method taught in Cronin, et al., the microarray is used to perform such hybridizations. Accordingly, the present invention as now defined with the newly presented claims 13-26, is novel and also based on an inventive step and distinguishable over of Cronin, et al.

Claim 12 stands rejected under 35 U.S.C. § 102 (b) as being anticipated by Ness et al (U.S. Patent No.6,027,890, issued 22 February 2000). The Examiner states that "Ness et al disclose the use of betaines as additives for solvents in which nucleic acids are dissolved in order to bind them to a carrier, i.e., Ness et al dissolves nucleic acids in triethylammonium acetate to separate the fragments via high performance Liquid chromatography in order to bind the separated fragments on to a carrier (Column 56, lines 3-33)."

The Ness, et al., reference describes "*methods and compositions for enhancing sensitivity in the analysis of biological-based assays*" (see title). Nucleic acids chips and protein chips are described in column 54, line 4 to column 56, line 2. In column 56, lines 25 and 26, the betaine "triethylammonim acetate" is described, but not in connection with the fabrication of microarrays, and more in particular not in connection with the spotting of nucleic acids. The betaine "triethylammonium acetate" is disclosed in Ness et al, in

connection with a method that uses High Performance Liquid Chromatography (HPLC). Such an HPLC-method is totally different from a process for making a microarray and the spotting of a spotting solution onto a carrier to bind nucleic acids.

Clearly, Ness et al. does not describe the use of betaines in making a "spotting solution" for binding nucleic acids to a carrier in order to make microarrays.

Thus, the present invention as now claimed in claims 13-26 is also novel and patentable over Ness et al.

It is respectfully requested that the rejections under 35 U.S.C. § 102(b) be withdrawn.

THE REJECTION UNDER 35 U.S.C. § 103(a)

The rejection of claims 1-3 under 35 U.S.C. 103 (a) as being unpatentable over Ness et al (U.S. Patent No. 6,027,890, issued 22 February 2000) is courteously traversed. The Examiner states the following:

"Regarding Claim 1, Ness et al teach a method for binding nucleic acids to a carrier wherein the nucleic acids are dissolved in a solvent containing at least one betaine i.e. Ness et al dissolves nucleic acids in triethylammoium acetate to separate the fragments (e.g. PCR products) via high performance liquid chromatography (HPLC) (Column 56, lines 3-33) and Ness et al. apply PCR products to the carrier whereby the nucleic acids are bound to the carrier (Column 74, lines 26-59 and Column 75, line 64-Column 76, line 8).

The teaching of Ness et al clearly suggest that the HPLC purified PCR are applied to the carrier. Following their suggestion, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply PCR products dissolved

in betaine and HPLC purified to the carrier of Ness et al for the obvious benefits of binding PCR products of correct size to the carrier as suggested by Ness et al (Column 56, lines 31-33).

Regarding Claim 2, Ness et al teach the method for binding nucleic acids to a carrier wherein the nucleic acids are dissolved in a solvent containing at least one betaine, applying the nucleic acid solution to the carrier whereby the nucleic acids are bound to the carrier i.e. Ness et al dissolves nucleic acids in triethylammonium acetate to separate the fragments (e.g. PCR products) via high performance liquid chromatography (Column 56, lines 3-33), the separate fragments (e.g. PCR products) in the obtained solution are then applied to a carrier to bind the nucleic acids thereto) Column 74, lines 26-59 and Column 75, line 62-Column 76, line 8) wherein the betaine is triethylammonium acetate but not trimethylammonium.

However, based on their similar physical and chemical similarities and absent unexpected results, one of ordinary skill in the art would have expected the triethylammonium acetate to function in a similar manner as the trimethylammonium.

Therefore one of ordinary skill in the art would have substituted the instantly claimed triethylammonium acetate for the triethylammonium of Ness et al based on the expected similar functionality.

Regarding Claim 3, Ness et al disclose the method wherein the betaine is present in the solvent at a concentration of 8 mM to 6.5 M (Column 56, lines 25-33).

Once again and as pointed out above, the Ness, et al., reference describes "*methods and compositions for enhancing sensitivity in the analysis of biological-based assays*" (see title). Nucleic acids chips and protein chips are described in column 54, line 4 to column 56, line 2. In column 56, lines 25 and 26, the betaine "triethylammonim acetate" is described, but not in connection with the fabrication of microarrays, and more in particular not in connection with the spotting of nucleic acids. The betaine "triethylammonium acetate" is disclosed in Ness et al, in connection with a method that uses High Performance Liquid Chromatography (HPLC). Ness et al. dissolves nucleic acids in triethylammonium acetate to separate the fragments (e.g. PCR products) via high performance liquid chromatography (Column 56, lines 3-33) Such an HPLC-method is totally different from a process for making a microarray and the spotting of a spotting solution onto a carrier to bind nucleic acids.

Clearly, Ness et al. does not describe the use of betaines in making a "spotting solution" for binding nucleic acids to a carrier in order to make microarrays. Ness et al. is silent regarding making a spotting solution and binding DNA to a carrier and making microarrays.

Thus, the present invention as now claimed in claims 13-26 is also novel and patentable over Ness et al.

It is respectfully requested that the rejections under 35 U.S.C. § 103(a) be withdrawn.

In view of the above amendments and remarks, it is respectfully submitted that the claims are now in condition for allowance. Reconsideration and withdrawal of the rejections and objections are requested. The Examiner is invited to contact the undersigned at 703-418-2777 if she feels that further discussion may facilitate the resolution of any outstanding issues. An early indication of a Notice of Allowance is earnestly solicited.

Respectfully submitted,

Telephone:
(610) 565-6090
Facsimile:
(610) 566-9790
P. O. Box 2056
205 North Monroe Street
Media, PA 19063-9056

EUGENE E. RENZ, JR.
Attorney of Record
Registration No. 19,557

Date: August 4, 2003

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